

FINAL PROGRESS REPORT FOR NASA GRANT NAG2-1326

OTOLITH-CANAL CONVERGENCE IN VESTIBULAR NUCLEI NEURONS

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Beginning Date: 6/1/99

Ending Date: 5/31/02

Institution: Central Institute for the Deaf, St. Louis, MO

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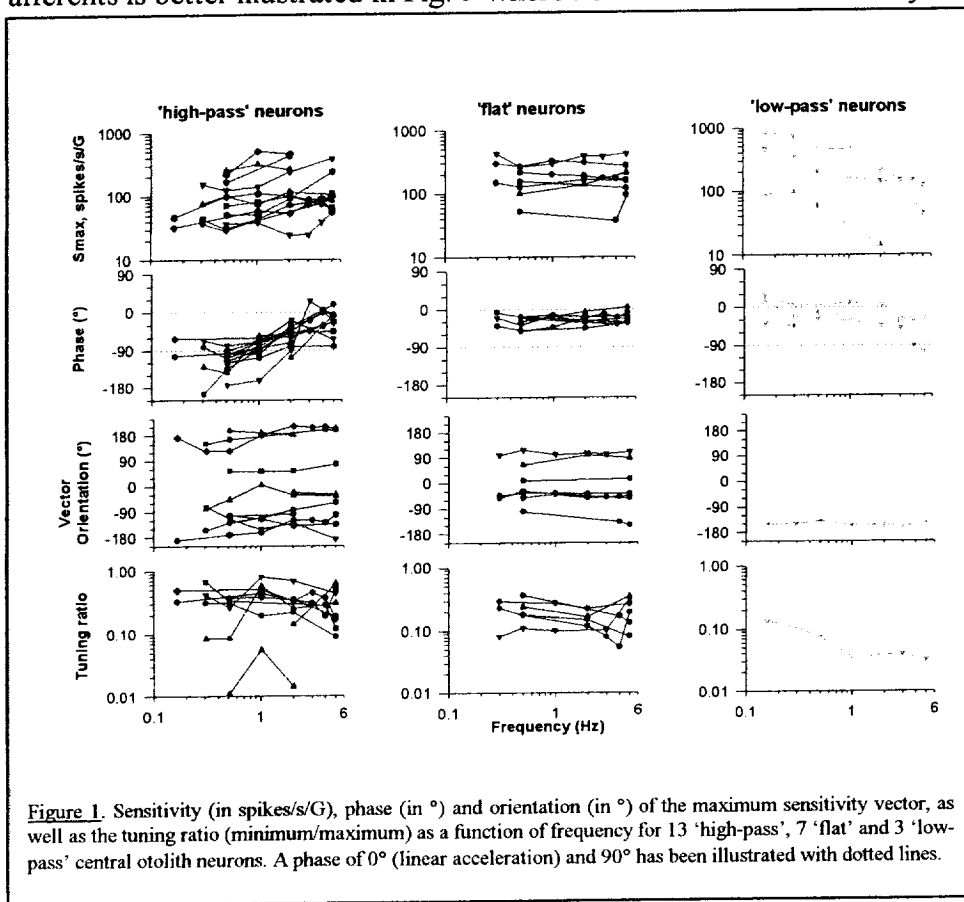
Description of Research:

The current final report covers the period from June 1, 1999 to May 31, 2002. The primary objective of the investigation was to determine how information regarding head movements and head position relative to gravity is received and processed by central vestibular nuclei neurons in the brainstem. Specialized receptors in the vestibular labyrinths of the inner ear function to detect angular and linear accelerations of the head, with receptors located in the semicircular canals transducing rotational head movements and receptors located in the otolith organs transducing changes in head position relative to gravity or linear accelerations of the head. The information from these different receptors is then transmitted to central vestibular nuclei neurons which process the input signals, then project the appropriate output information to the eye, head, and body musculature motor neurons to control compensatory reflexes. Although a number of studies have reported on the responsiveness of vestibular nuclei neurons, it has not yet been possible to determine precisely how these cells combine the information from the different angular and linear acceleration receptors into a correct neural output signal. In the present project, rotational and linear motion stimuli were separately delivered while recording responses from vestibular nuclei neurons that were characterized according to direct input from the labyrinth and eye movement sensitivity. Responses from neurons receiving convergent input from the semicircular canals and otolith organs were quantified and compared to non-convergent neurons.

Accomplishments:

Response dynamics of otolith afferents and central otolith neurons. In primates, vestibular nuclei neurons can be characterized by their sensitivity to head motion, eye movement, and body movement. One class of central vestibular neurons, termed vestibular only (VO) cells, can be identified by their lack of response to either static eye position or dynamic eye movements in monkeys that were pre-trained to fixate visual targets for juice reward. During this portion of the project, we recorded from a number of central vestibular VO neurons in rhesus monkeys and classified them according to their response sensitivities. We first analyzed and reported upon central VO neurons responding to linear motion only, termed otolith-only neurons. In addition to the central otolith-only neurons, primary otolith afferents were also recorded in the monkeys to serve as a comparison. Each afferent and OT neurons were studied

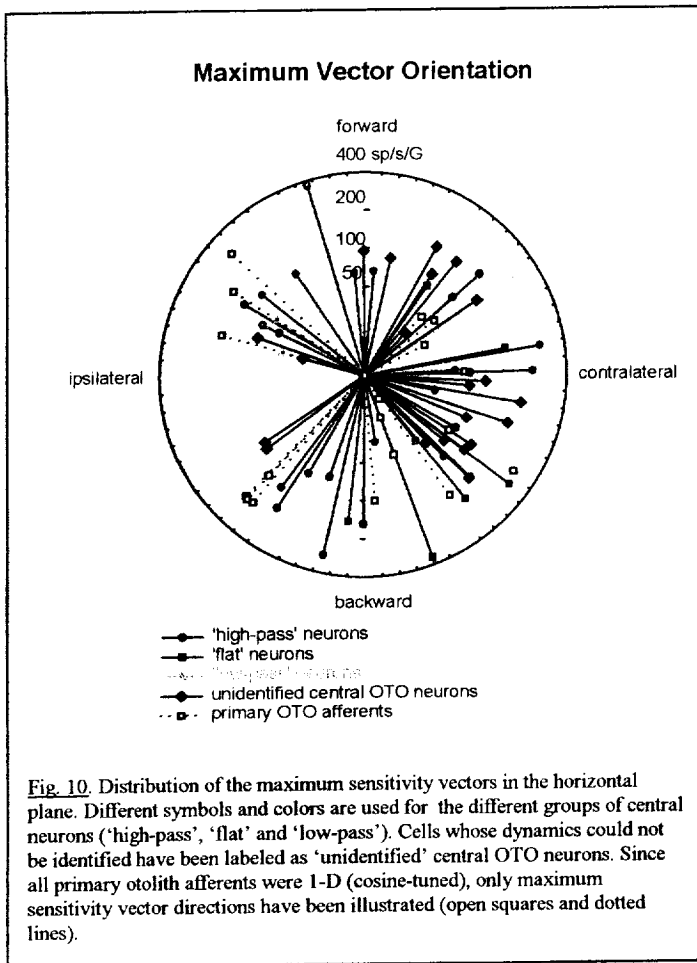
using linear acceleration stimuli delivered along different orientations relative to head position and at different frequencies. The primary orientations for stimulation were linear motion directed along the naso-occipital and interaural axes. The frequencies used ranged between 0.15 and 10 Hz, with an amplitude of 0.2 or 0.3g. For the 23 central otolith neurons studied, groups of cells with three distinctly different response dynamics were observed. As shown in Fig. 1 (left), the majority of cells (13/23, 57%), termed 'high-pass' neurons, had gains that increased with frequency and phases that significantly lagged linear acceleration at low frequencies (phase $< -60^\circ$ at frequencies of ≤ 0.5 Hz). A second group of cells (7/23, 30%; Fig. 1, middle), termed 'flat' neurons, were characterized by relatively constant sensitivities and phase lags (ranging from -55° to $\sim 0^\circ$) for all stimulus frequencies. A third group of central otolith neurons (3/23, 13%; Fig. 1, right) exhibited maximum sensitivities that decreased with frequency and phase lags that increased with frequency. We refer to these cells as 'low-pass' neurons. The difference in the response dynamics between these groups of central neurons and in relation to those of primary otolith afferents is better illustrated in Fig. 9 where normalized mean sensitivity and phase have been plotted



versus frequency. It is apparent that although there is a large range in central otolith dynamics, none of the three groups have responses that are characteristic of primary otolith afferents. The changes in sensitivity as a function of frequency were usually more extreme than afferents and phase values had larger lags than those of otolith afferents at nearly all frequencies.

Spatial and temporal response properties of otolith only vestibular neurons: The otolith afferents and OT neurons were also studied using linear translations

sinusoidally oscillated at different directions in an Earth horizontal plane. Two stimulus protocols were used. First, the maximum sensitivity direction for each OT neuron was determined by delivering 0.5 and 2.0 Hz, 0.2g linear translations with the animals being placed at 7 different orientations relative to the stimulus axis. The 7 orientation positions were indexed at 15° intervals and all lay within the horizontal head plane. The responses obtained from these positions were then used to determine a maximum response direction for each otolith only cell, by plotting the response gain and phase values as a function of head position and fitting a modified cosine curve. The direction of linear acceleration that produced the maximal response differed for each neuron. The distribution of the maximum vector directions for the



contralaterally. We did not encounter any neuron whose maximum sensitivity direction was pointing within $\pm 15^\circ$ from the ipsilateral ear. These response vectors coincide well with the known morphological polarizations of hair cell stereocilia on the utricular maculae. Thus, the OT neurons are most sensitive to side-to-side head movements, or small head tilts away from earth vertical.

Spatial response properties of canal-only and otolith + canal neurons: A number of central neurons were obtained that had different convergent properties. Two additional major groups of VO cells were identified, with Canal-only neurons responding to rotational motion only and Otolith + canal neurons responding to rotational motion about an earth vertical axis (to eliminate simultaneous otolith stimulation) and to linear motion. The 3D maximum sensitivity directions to rotational motion were calculated for 40 Canal-Only and 48 Otolith+Canal neurons, where sufficient earth-vertical axis (EVA) rotations about multiple directions were obtained. These unity-sensitivity orientation vectors were plotted as projections onto the three cardinal head planes, as shown in Fig. 3 and 4. Differences in the response vector distributions were striking, with a statistically significant difference in the rotational maximum sensitivity vector directions for Canal-Only and Otolith+Canal neurons ($F(3,83)=12.0$, $p<0.01$). As shown in Fig. 3, Canal-Only neurons that do not respond during translation have maximum sensitivity vectors that are closely aligned with those of the semicircular canal afferents. For comparison, the mean vector orientations of the horizontal canal (HC), anterior canal (AC) and posterior canal (PC) afferents in rhesus monkeys were also plotted (Fig. 3; red, green and cyan lines, respectively; Dickman et al. 2002). Of the 40 Canal-Only neurons in our sample, only 4 cells had vectors closely aligned with the HC. The

56 central otolith cells and 18 primary otolith afferents that were tested at different orientations are shown in Fig. 2. Four groups of central otolith neurons have been plotted. 'High-pass' neurons ($n=25$) included the 13 cells shown in Fig. 1, plus twelve additional neurons that had phase lags $\geq 60^\circ$ at 0.5 Hz (but were not tested across a broad enough frequency range to be included in the transfer function analysis). 'Flat' and 'low-pass' central neurons were those displayed in Fig. 1 ($n=7$ and $n=3$, respectively). The remaining ($n=21$) central otolith neurons were tested at only one or two frequencies and had sensitivity and phase values that would not allow sufficient characterization in terms of response dynamics. They were, thus, termed 'unidentified central OTO neurons'.

As shown in Fig. 2, the majority of the afferent and central cells had vectors pointing towards the contralateral ear. As a general rule, the 'high-pass' and the few 'low-pass' neural vectors were split between ipsilateral and contralateral. In contrast, the vectors of 'flat' central neurons tended to point mostly

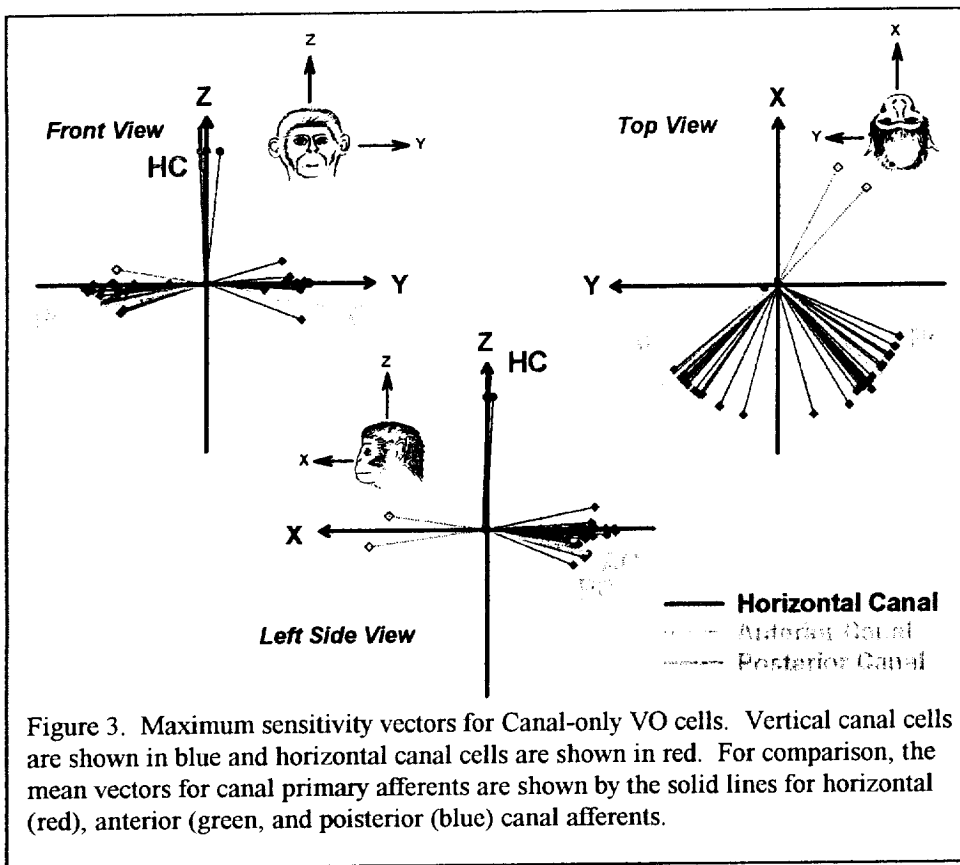


Figure 3. Maximum sensitivity vectors for Canal-only VO cells. Vertical canal cells are shown in blue and horizontal canal cells are shown in red. For comparison, the mean vectors for canal primary afferents are shown by the solid lines for horizontal (red), anterior (green, and posterior (blue) canal afferents.

majority of the sampled cells that did not respond to translation received inputs from only the vertical canals. Of these, 14 cells had vectors that were closely aligned with the ipsilateral AC, 20 cells had vectors closely aligned with the ipsilateral PC and 2 cells exhibited type II AC responses (i.e., their vectors were aligned with the contralateral AC).

As shown in Fig. 4, the distribution of rotational maximum sensitivity vectors of the Otolith+Canal convergent neurons was substantially more dispersed than Canal-Only cells. When viewed in total as a group,

these neurons had vectors that were uniformly distributed throughout the 3D space. During the recording sessions, an attempt was made to qualitatively characterize neurons as type I HC, type II HC and VC neurons (depending on their excitability and phase during yaw rotations in upright, as well as nose-up and nose-down orientations; see Methods). This on-line characterization is reflected in the color, lines and symbols used in the plots of Fig. 4. As expected, HC type convergent neurons generally lay within 45° of the z-axis. Conversely, VC neurons had vectors mostly located within 45° of the x-y plane. However, since we found no difference in any of the response properties (including the gain, phase of either rotational or translational responses, as well as in the relationship between rotational and translation responses; $p > 0.05$) between type I HC, type II HC and VC neurons, all cells were grouped as Otolith+Canal neurons for further analyses.

Dynamics of convergent neurons: The dynamic properties of the Otolith+Canal neurons were similar to those observed for Otolith-Only neurons (Angelaki and Dickman 2000), as shown in Fig. 5. In general, response dynamics differed for stimulation along different directions of translation, as previously described (Angelaki and Dickman 2000). Since many VN neurons exhibited spatiotemporal convergence, only the gain and phase values obtained for translation along the maximum sensitivity directions were illustrated. Similar to Otolith-Only neurons, Otolith+Canal neurons exhibited a wide range of response dynamics to translation. For example, the gains either remained flat, increased or decreased as a function of stimulus frequency (Fig. 5). Response phases differed greatly at low frequencies and were typically in-between velocity and acceleration at high frequencies. Neurons with large phase advances versus frequency ($>90^\circ$) generally had either increasing or relatively flat gains (Fig. 5A). Neurons whose phase remained relatively constant between linear velocity and acceleration exhibited relatively flat gains (Fig. 5B). Finally, approximately one third of the neurons exhibited gains that decreased with frequency and phase behavior that varied greatly (Fig. 5C). These response characteristics are similar to those previously

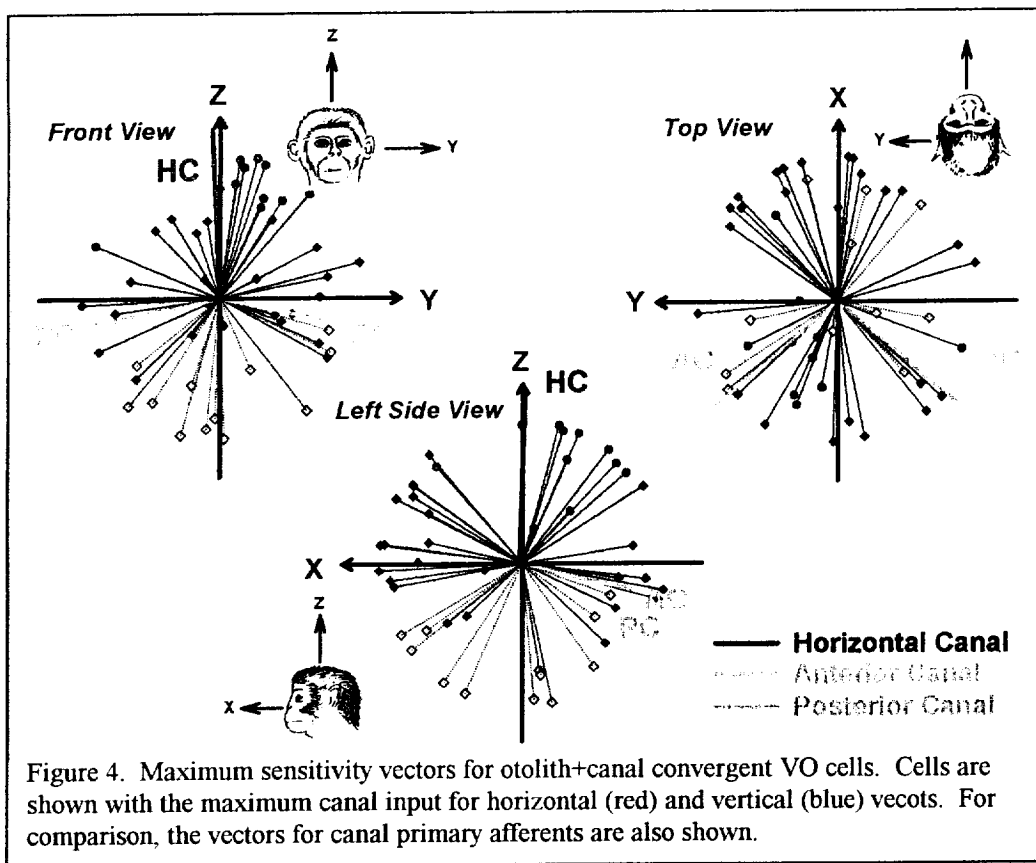


Figure 4. Maximum sensitivity vectors for otolith+canal convergent VO cells. Cells are shown with the maximum canal input for horizontal (red) and vertical (blue) vecots. For comparison, the vectors for canal primary afferents are also shown.

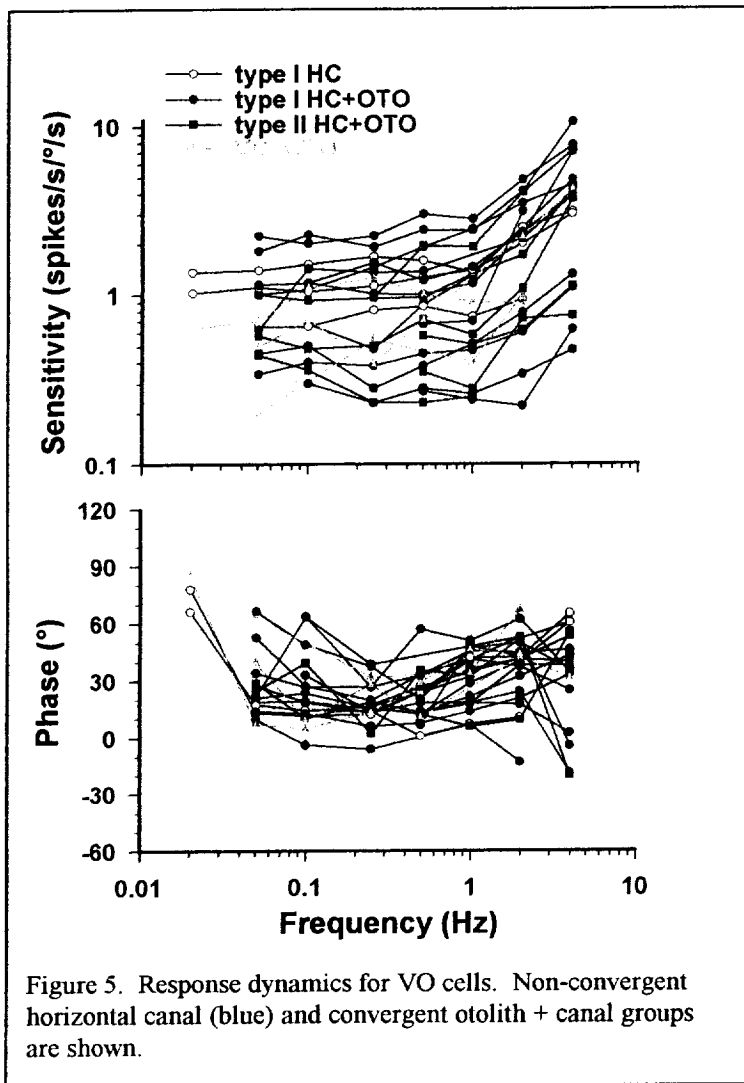
reported for Otolith-Only cells (Angelaki and Dickman 2000) and suggest that the spatiotemporal processing of vestibular signals during head translation are similar for Otolith-Only and Otolith+Canal neurons.

Relationship between Rotational and Translational response sensitivity vectors:

During natural vertical plane rotations, both otolith and semicircular canal afferents are simultaneously activated. For example,

during pitch head movements from an upright position, primary otolith afferents with maximum sensitivity vectors close to the naso-occipital axis will be co-activated along with vertical SCC afferents. Because of such a complementary activation, it was of interest to examine if a systematic spatial relationship existed between the rotational and translational vectors for the Otolith+Canal convergent neurons. Thus, a 'Canal vector angle' was calculated as the angle formed between the projection of the 3D rotational sensitivity vector onto the horizontal x-y plane and the positive x-axis. Next, an 'otolith rotation vector angle' was also computed as the axis of rotation about which the head had to be rotated in a vertical plane in order to place the translational sensitivity vector of the cell in the plane of rotation (computed by rotating the translational maximum sensitivity vector of the cell through 90°). We considered that it was possible that the translation/tilt sensitivity direction of convergent VN cells could be aligned with the canal rotational sensitivity direction. Such a hypothesis would be based on the following two presumptions. First, Otolith+Canal convergent neurons respond to tilts of the head relative to gravity in a manner equivalent as during translation, similar to otolith afferents and Otolith-Only neurons (Angelaki and Dickman 2000). Second, otolith/canal convergence should function to 'augment' or 'supplement' rotational response sensitivity during natural tilts from upright.

The relationship between the computed 'otolith rotation vector angle' and the 'canal vector angle' was compared. If the translational and rotational directional tunings for each cell were complementary, the data should fall along the unity-slope (dotted) line. For most of the Otolith+Canal convergent neurons, no such relationship between the two angles was observed. In fact, for only 9/44 (20%) cells the computed angles were within $\pm 30^\circ$ of the unity-slope line. These findings in primate VN neurons appear to be different from that previously reported for lateral-eyed species, suggesting that otolith/canal convergence in primates might subserve a different function (Angelaki et al. 1993).



Publications from NAG2-1326:

Abstracts

- Dickman, J.D., McHenry, M.Q., and Angelaki, D.E. Vestibular neuron responses to linear motion in alert rhesus monkeys. *Soc. Neuroscience Abst.*, 1998, 24, 1653.
- Dickman, J.D. and Angelaki, D.E. Convergence of semicircular canal and otolith information to vestibular neurons in alert rhesus monkeys. *Association for Research in Otolaryngology Abst.*, 1999, 22, 103.
- Haque, A., Dickman, J.D., and Angelaki, D.E. 3D orientation and dynamics of vestibular semicircular canal afferents in rhesus monkeys. *Soc. Neuroscience Abst.*, 1999.
- Dickman, J.D. and Angelaki, D.E. Properties of afferent convergence for central vestibular neurons in alert rhesus monkeys. *Soc. Neuroscience Abst.*, 1999.

- Dickman, J.D. and Angelaki, D.E. Properties of afferent and central otolith neuron responses to linear motion in alert rhesus monkeys. *Soc. Neuroscience Abst.*, 2000.
- Green, A.M., Dickman, J.D., and Angelaki, D.E. Canal and otolith cues for detecting motion: theories of brainstem neural coding. *Society for the Neural Control of Movement Abstract*, Naples, FL., April, 2002.

Articles

- Angelaki, D.E. and Dickman, J.D. Spatiotemporal processing of linear acceleration: primary afferent and central vestibular neuron responses. *J. Neurophysiol.*, 2000, 84, 2113-2132..
- Angelaki, D.E., McHenry, M.Q., Dickman, J.D., Newlands, S.D., and Hess, B.J.M. Computation of inertial motion: Neural strategies to resolve ambiguous otolith information. *J. Neuroscience*, 1999, 19, 316-327.
- Dickman, J.D., Haque, A. and Angelaki, D.E. Dynamics of primate vestibular neurons during rotation. *J. Neurophysiol.*, 2002 (in press).
- Dickman, J.D. and Angelaki, D.E. Neural coding of 3D rotational and translational motion: Convergence patterns of vestibular signals in the primate brainstem. *J. Neuroscience*, 2002, (under review).